DISPENSING APPARATUS AND METHOD FOR LIQUID PRODUCTS, PARTICULARLY MEDICINAL PRODUCTS

The present invention concerns a dispensing apparatus for liquid products, particularly medicinal products, such as an ophthalmic solution.

Although the principles of the present invention may have utility in many areas, for convenience it will be described mainly in connection with liquid treatment of eyes. Typically the medical preparation has to be delivered in a fairly well defined volume to assure a specified dose to be delivered or absorbed. A large surplus cannot be allowed due to improper systemic physiological effects from absorbency in non-target tissues or drainage of excess amounts through the tear channel into the throat cavity or the inconveniences caused by overflow on face and clothes. Also price considerations apply for expensive medications. As an example, the treatment of glaucoma requires frequent daily administrations of e.g. prostaglandins, beta-blockers or other expensive active ingredients, all having other then the desired pressure relieving action when absorbed by other body tissues than the eye. Small volume dosing is negatively affected by even small uncontrolled or dead spaces in delivery equipments used. Moreover, medical preparation components may be sensitive to degradation or absorption at prolonged exposure to materials and extended surfaces present in delivery devices. Similar considerations apply for sterility preservation. With regard to stream quality, proper administration of small amounts is complicated by the fact that the active ingredients cannot enter the eye but through the limited area of the cornea. It is also necessary that the entire dose can be delivered before the triggered blink reflex closes the eyelid.

A large number of devices are already known for applying a determined quantity of a liquid medicinal product onto a part of the body, such as an ophthalmic solution on the surface of the eye. These devices generally rely on the principle of a syringe which can be either pre-filled with a determined quantity of liquid, or graduated to suck up said quantity of liquid contained in a separate bottle, or connected to a fixed receptacle in permanent communication with the dosing chamber of the syringe, as is described for example in one of the embodiments of US Patent No. 4,623,337. It will be observed that permanently feeding the dosing chamber from the receptacle via gravity means that neither the precision of the quantity of liquid to be ejected, nor the sterility thereof can be guaranteed. In these devices, the pressure exerted on the plunger, manually or automatically, is generally exerted in the same direction as that of the liquid jet, as is described for example in International Patent Application No. WO 92/20455.

The direction of the jet can sometimes be deviated by bent conduits, but it is then difficult to control the force with which the jet reaches its target. A device of this kind is like, for example, that disclosed in French Patent No. FR 2 647 757 for food products or cosmetics in liquid or paste-like form, for which respecting a given ejection pressure is of no importance.

In the case of a an ophthalmic solution, it is, however, very important not only to control very precisely the dose to be ejected for obvious reasons of safety and efficacy of the treatment, but also in order to be able to control the impact pressure of the liquid jet on the eye, which certain devices attempt to achieve by using an eyepiece or a spacing member applied to the periphery of the target to impose a fixed distance with respect to the liquid ejection orifice, as is disclosed for example in US Patent Nos. 4,623,337 and 5,836,911. It will be observed however that these devices do not always allow the impact force of the liquid jet to be reproduced when the pressure is exerted directly on the plunger manually.

Thus, the dispensing apparatuses of the prior art provide individual solutions to particular problems, but none of them allows all of the aforementioned problems to be simultaneously resolved.

The object of the present invention is thus to provide a dispensing method and device capable of avoiding the problems discussed above. More particularly an object is to provide a method and device system capable of ejecting, e.g. with a new design of the plunger head leaving practically no ullage, a precise dose of liquid, such as an ophthalmic solution, with an adjustable impact pressure on the target and the dose and impact pressure being independent of the way in which the pressure is exerted on the actuator. The apparatus according to the invention includes a mechanism allowing sterility conditions to be improved, given that the receptacle is only in communication with the dosing chamber except for a brief moment during ejection when it is placed in communication with the external environment for a few tenths of a second, during which time the pressure equilibrium is achieved by replacing the sucked up liquid with air. In addition the system allows uncontrolled and adead spaces to be kept to a minimum. The apparatus is further very easy to use in particular for an ophthalmic solution.

These and other objects are reached by the characteristics set forth in the appended patent claims.

The movement of the actuator is preferably substantially perpendicular to the direction of ejection of the liquid, such that the pressure exerted on the actuator cannot modify the distance with respect to the target, for example the eye in the case of an dispensing ophthalmic solution.

According to a first embodiment, the mobile element is formed by a drum provided, on its flanks, with studs rotatably mounted in the two shells of the housing, and housing in its diametral part an assembly formed by the dosing chamber, the plunger and the return spring.

At the start of pressure on the actuator, the drum occupies a first filling position in which the orifice of the dosing chamber is opposite the receptacle feed nozzle. By continuing to press on the actuator, the drum rotates through an angle α to occupy a second ejection position in which the orifice of the dosing chamber is opposite the through passage of the housing.

In a second embodiment, the dosing chamber is formed in a unit secured to the frame, and the mobile element is formed by a mobile valve, held in the rest position by a return spring. At the start of pressure on the actuator, the valve occupies a first position for filling the dosing chamber through a channel formed in the thickness of said valve placing the orifice of the dosing chamber in communication with the receptacle nozzle. By continuing to press on the actuator the valve is brought into a second ejection position in which the orifice of the dosing chamber is placed in communication with the exterior through a hole of the valve located opposite the through passage of the frame.

In both embodiments, the actuator is returned to the rest position by resilient return means, wound by the travel of the plunger during the filling and ejection phases. In these two embodiments, in order to further increase the conditions of sterility, the actuator can include a panel blocking the through passage of the housing or frame from the exterior in the rest position, said panel including an orifice brought to face said through passage in the ejection position.

Other features and advantages of the present invention will appear more clearly upon reading embodiment examples, given purely by way of non-limiting illustration, with reference to the annexed drawings, in which:

- Figure 1 shows a perspective view of a dispensing apparatus according to the invention without the external cover;
- Figure 2 shows a cross-section of the apparatus of Figure 1, along the arrows II-II parallel to the base of the apparatus;
- Figure 3 shows an exploded perspective view of the apparatus of Figure 1;
- Figure 4 shows a side view of the apparatus of Figure 1 in which one shell of the housing and the drum have been removed;
- Figure 5 shows a cross-section along the line V-V of Figure 2, of the mechanism assembly in the rest position;

- Figure 6 corresponds to the suction phase of a determined quantity of liquid to be ejected;

- Figure 7 corresponds to the rotation of the drum to the ejection position;

- Figure 8 corresponds to the liquid ejection phase;

- Figure 9 shows a position of the drum during the return to its rest position;

- Figures 5A to 9A show the different positions of the drive members in the phases corresponding to Figures 5 to 9;

- Figure 10 shows a side view of a second embodiment of the invention;

- Figure 11 is a cross-section in the plane of symmetry of the apparatus shown in Figure 10 in the rest position;

- Figure 12 is an exploded perspective view of the apparatus shown in Figure 10;

- Figures 12A and 12C are enlarged diagrams of two elements of the mechanism from another angle;

- Figure 12B is a cross-section of another element of the mechanism;

- Figure 13 corresponds to the suction phase of a determined quantity of liquid;

- Figure 13A is an enlarged diagram of the valve during the liquid suction phase;

- Figure 14 shows the phase during which the valve passes into the liquid ejection phase;

- Figure 14A is an enlarged diagram of the valve during the liquid ejection phase;

- Figure 15 shows the liquid ejection phase;

- Figures 16, 17, 18 show the return of the apparatus to the rest position; and

- Figures 19, 19A and 20 respectively show in the rest position and at the end of ejection a variant illustrated with the second embodiment.

In Figure 1, Figures 1 and 10 show, in perspective, two embodiment examples of a dispensing apparatus according to the invention. In Figure 1, the apparatus includes an external cover 1 marking the mechanism of a second embodiment which will be described hereinafter where the external cover has been removed, one can see that externally the apparatus includes a housing 2 formed of two shells 2a, 2b assembled by a screw 2c after positioning the contact surfaces by means of pins 2d visible in the exploded view of Figure 3, to which reference will also be made in the description hereinafter. The liquid, which will have to be ejected from the apparatus in the direction of double arrow L, is contained in a receptacle 4 which, in this example, is a bottle ending in a feed nozzle 4a. Bottle 4 is secured to the apparatus by means of an adjustable clamp 5, to shells 2a, 2b by means of screws 5a. In Figure 1, it can also be

seen that actuator 30, the actuation of which by a force F is effected in a substantially perpendicular direction to the direction of ejection of the liquid. In this embodiment, the actuator take the form of a push button and is generally U-shaped with a head 32 extended by two branches 34a, 34b, the construction and functions of which will be described hereinafter.

Reference will also now be made to Figure 4, in which external cover 1 has been kept, but shell 2b and drum 50 have been removed. Drum 50 forms, with the parts which drive it in one direction or another, the main mobile element of the mechanism according to the invention. Drum 50 includes on each of its flanks 52a, 52b studs 54a, 54b rotatably mounted in bearings 44a, 44b provided in the inner faces of shells 2a, 2b. Drum 50 also includes at its periphery an opening 56 corresponding to a through passage in which dosing chamber 11 will be mounted, provided with an ejection orifice 11a, a plunger 10 comprising a head 12, and a rod 13 having a groove 13a at its end. The particular structure of head 12, which contributes to the precision of the quantity of liquid ejected and to the non-contamination of the chamber by external polluting agents will be explained in more detail with reference to the second embodiment.

The drum also includes a slit 58 in which two lateral arms 22a, 22b of a staple 20 are engaged, said staple being snapped into groove 13a of rod 13, by compressing a spring 14 mounted on rod 13 of plunger 10, when said staple 20 is moved, from the bottom of slit 58 to the edge of drum 50. The movement of staple 20 is achieved by a double lever 24, articulated in its median part in shells 2a, 2b, each lever including an arm 26a pressing on each lateral arm 22a, 22b of staple 20. Each arm 26a of double lever 24 also includes a snug 28, allowing a safety catch 62 to be manoeuvred.

In proximity to slit 58, drum 50 also includes a notch 64 in which safety catch 62 will be engaged, the function of said catch being described hereinafter within the scope of the description of the working of the apparatus. Finally, drum 50 includes on each of its flanks 52a, 52b, two bean-shaped holes 66a, 66b, the function of which is explained hereinafter.

On each of studs 54a, 54b of drum 50 there is mounted a pinion 60, each pinion including along its axis two pins 61a, 61b, more clearly visible in enlarged Figure 3A. When a pinion 60 is mounted on a stud 54a, 54b of the drum, pins 61a, 61b are engaged in holes 66a, 66b, such that, when pinion 60 is driven in rotation, it has a small angle of shake during which drum 50 is not driven in rotation.

In Figure 4, it can be seen that pinions 60 mesh with the toothings, on the one hand, of actuator 30, and of a return member 40 on the other hand.

As indicated at the beginning, the actuator includes symmetrical branches 34a, 34b, the spacing of which substantially corresponds to the width of the drum. Each branch 34a, 34b is formed of an external part ending in a stop member 36, for manoeuvring arms 26b of lever 24, and of an internal part formed by a straight rack 38 extending on either side of stop member 36 in the longitudinal direction of branches 34a, 34b.

Return member 40 is formed by a double pivoting rack including two branches 40a, 40b connected by a bridge 42, the pivoting rack being articulated in shells 2a, 2b of housing 2. A return spring 46 allows the double rack to be kept in the low position when there is no pressure exerted on actuator 30 and to return it to this position when the actuator is released after having exerted pressure on the latter.

Finally, it can be seen that the inner surfaces of shells 2a, 2b each include a cam 6 having the shape of an arcuate rib. The end 22a, 22b of the lateral arms of staple 20 are capable of sliding on the external contour of rib 6 in order to keep spring 14 compressed during the rotation of drum 50 between the filling position and the ejection position. In the example illustrated cam 6 extends over an angle of approximately 120°.

The parts which have just been described, essentially with reference to the exploded view of Figure 3, appear at least partially in the cross-section of Figure 2 where the mechanism is shown with its external cover 1 and a sliding member 8 for adjusting the distance between the ejection orifice and an eyepiece 8a located at its end. Sliding member 8 and eyepiece 8a are shown in two end positions in Figure 4. Figure 3 also shows the cross-section line V-V corresponding to Figures 5 to 9 which will now enable the operation of the mechanism to be explained.

The operation of this first embodiment is now described with reference to Figures 5 to 9.

Rest position (Figures 5 and 5A)

No pressure is exerted on actuator 30. Safety catch 62 is engaged in notch 64 of drum 50 and the orifice of dosing chamber 11 is opposite the nozzle of receptacle 4. Spring 46 rests on return rack 40, keeping pins 61a, 61b in the low position in holes 66a, 66b. The two ends of lever 24 are abutting respectively against stop member 36 and staple 20. As the plunger head is pressed against the bottom of the dosing chamber, receptacle 4 is perfectly insulated from the external environment, and leaves no ullage.

Dosing chamber filling position (Figures 6 and 6A)

By exerting a pressure F on actuator 30, stop member 36 tips lever 24, and rack 38 drives pinion 60 to a high position in which pins 61a, 61b do not drive drum 50. In this step lever 24 pulls plunger 10 thus sucking up the liquid from bottle 4 to fill the dosing chamber to a position where staple 20 is placed behind cam 6. At this moment snug 28 of lever 24 pushes back safety catch 62 releasing drum 50. In this phase, spring 46 starts to be compressed.

Passage into the ejection position (Figures 7 and 7A)

By continuing to exert pressure F on actuator 30, rack 38 drives pinion 60 which itself rotates drum 50, by means of pins 61a, 61b which rest on one end of holes 66a, 66b. During this rotation, staple 20 follows via its lateral arms the external contour of the rib forming cam 6. Figure 7 shows the position just preceding ejection, orifice 11a of dosing chamber 11 being substantially on the axis of ejection. Rack 40 then exerts maximum compression on spring 46.

The ejection position (Figures 8 and 8A)

By exerting an additional pressure, the lateral arms of staple 20 go beyond the end of cam 6 so that the staple is no longer held. Return spring 14 of plunger 10 then pushes the plunger head to the end of dosing chamber 11 to eject the liquid. In this phase it will be observed that the pressure with which the liquid is ejected depends solely upon the characteristics chosen for spring 14, and in no way upon those of return spring 46, nor the manner in which the user exerts force F.

It will also be observed that, if the user does not reach this ejection position by releasing pressure F during filling or rotation of the drum, the dosing chamber is returned to its initial position and the unused product is re-injected into the receptacle. This constitutes a certain advantage when the product is a medicinal one whose price is generally high.

Return to the rest position (Figures 9 and 9A)

By releasing the pressure after ejecting the liquid, return spring 46 tips rack 40 in the opposite direction driving drum 50 via pinion 60 whose pins 61, 61b are stopped

at the other end of holes 66a, 66b. At the end of rotation, drum 50 again occupies the position shown in Figure 5. The apparatus is again in position for a new use.

With reference now to Figures 10 to 18, a second embodiment will be described hereinafter, in which the mobile element is formed by a valve 51, able to be moved by the action of the actuator, along the same direction as the latter, to place, in a first phase, the receptacle containing the liquid in communication with the dosing chamber, then, in the second phase, in communication with the exterior.

The side view of Figure 10 shows a dispensing apparatus with the same external appearance as the previously described apparatus, and wherein the entire mechanism is masked by external cover 1, leaving only actuator 30 visible, itself including an external cover 30a, bottle 4 forming the receptacle containing a liquid, for example an ophthalmic solution, and slide 8 with its eyepiece 8a.

The actual mechanism will now be described, referring essentially to Figures 11 and 12. It can be seen that the mechanism is assembled by means of frame 3 for receiving a unit 9 in which the dosing chamber is formed, more clearly visible in Figure 13A. Actuator 30 includes, perpendicular to its head 32, a plate 31 provided with an aperture 31a, and perpendicular to said plate a thick rib 33 including a snap-fitting groove 33a for a tipping element 41, having a reverse L shape, an enlarged perspective of which is shown in Figure 12A. L-shaped element 41 forms the control member which acts, in a first movement phase of actuator 30, on means for actuating plunger 10 against the action of a return spring 14, and in a second phase on a valve 51 able to move in the same direction as actuator 30, against the action of return springs 53a, 53b disposed between said valve 51 and frame 3. As can be seen more clearly in enlarged Figure 12A, L-shaped tipping element 41 includes a recess 41a, for receiving one end of a helical spring 47 and the other end of which is held abutting against thick rib 33 by means of a spacer 47a.

Spring 47 is intended to hold element 41 abutting against a face of plate 31 during the active phase of actuator 30, then to be compressed during the return to the rest phase to allow said element 41 to tip and move aside behind the control member of plunger 10. The junction between the small branch 43 and large branch 45 includes on each of its edges pivots 45a allowing rib 33 to snap fit into groove 33a. Large branch 45 includes, in its substantially median part, an aperture 45b opposite aperture 31a of plate 31. At its base, branch 45 includes a corner shape 35 defining on the exterior an inclined plane 35a and in the interior two inclined ramps 35b parallel to inclined plane 35a and the width of which is substantially the same as the length of pivots 45a.

Valve 51, which can move in sliding channels 19 of unit 9 is described in more detail with reference to enlarged Figures 12C and 13A. It is formed of a parallelepiped body including two edges 51a in which two grooves 51b are formed, allowing sliding on slide ways 19 of unit 9. Its base includes an edge which includes small circular recesses 55a, 55b directed downwards to position return springs 53a, 53b.

The surface delimited by the two edges 51a and pressed against the surface opposite unit 9, includes at its centre an aperture 57 and a channel 59 whose ends 59a, 59b are located on either side of aperture 57 in the plane of symmetry of valve 51. Aperture 57 is surrounded by an inner O ring joint 69a and channel 59 by an outer O ring joint 69b, these joints 69a, 69b assuring sealing during movement of the valve. The longitudinal cross-section of Figure 13A shows the filling position in which nozzle 4a of receptacle 4 is placed in communication with orifice 11a of dosing chamber 11, by ends 59a, 59b of channel 59, which preferably has the shape of the arc of a circle. Figure 14A shows the ejection position in which aperture 57 of the valve is brought opposite orifice 11a of dosing chamber 11, nozzle 4a then be blocked by the surface of valve 51.

The actuating means for plunger 10, shown in cross-section in Figure 12B is formed by a clamp 21 including two large arms 23a, 23b ending in two lugs 29a, 29b the spacing of which substantially corresponds to the width of unit 9. The large arms 23a, 23b are connected by a base 27 including a hole 27a for securing rod 13 of plunger 10 and a recess 27b for positioning return spring 14. Lugs 29a, 29b each include two chamfers 25a, 25b having substantially the same inclination as inclined planes 35a, 35b of L-shaped tipping element 41. As will be explained hereinafter for the operation of the device, chamfers 25a, 25b each co-operate with inclined planes 35a, 35b, in a first phase, to act on plunger 10 filling dosing chamber 11 and, in the second phase, to allow the device to return to the rest position.

The cross-section of Figure 12B also shows a new design of plunger head 12 providing both greater precision in the suction/ejection of a determined quantity of liquid, and safety as regards contaminating elements able to come from the exterior through the sliding cylinder of the plunger. Plunger head 12 is formed of two parts 16, 17 assembled by an assembling member 18 having the form of a rod provided with a head 18a and a collar. The first part 16 has the shape of an inverted double cone 16a, 16b through which assembling member 18 passes, to secure it in rod 13, on the side of cone 16a. This first part 16 is made of a hard plastic material, such as polypropylene (OP) or polyethylene (PE). The second part 17 is formed by a sealing gasket 17, made of a flexible plastic material, such as a thermoplastic elastomer (TPE) or silicon, disposed in the second inverted cone 16b to fit into head 18a of pin 18. The external

part of gasket 17 has a hemispheric shape substantially corresponding to the shape of the bottom wall of the dosing chamber, as can be seen in Figures 13A and 14A. This design allows no ullage to be left during ejection of the liquid, and thus a precise quantity of liquid to be ejected, which is particularly important for medicinal products, and particularly ophthalmic solutions. The lips (not referenced) of inverted double cones 16a, 16b enable external polluting agents to be confined at the depression of their junction.

Plunger 10 which has just been described, for this second embodiment is also that found in the first embodiment described hereinbefore. It is clear that this plunger constitutes a preferred embodiment allowing the objectives of precision and sterility to be achieved for the dispensing apparatus according to the invention, but other types of plunger can be used without departing from the scope of the mechanisms which have just been described, and the operation of which is explained in more detail with reference to Figures 13 to 18.

Filling position (Figures 13 and 13A)

From the rest position shown in Figure 11, exerting a pressure F on the head of actuator 30, the inclined plane 35a of L-shaped tipping element 41 slides the corresponding chamfer 25a of clamp 21, pushing back plunger 10 and compressing spring 14. In this position the base 4a of the receptacle is in communication with the orifice of dosing chamber 11 via channel 59 and enables dosing chamber 11 to be filled.

Passage into the ejection position (Figures 14 and 14A)

By continuing to exert pressure F, the ends 43a of small arm 43 of the L-shaped tipping element press on valve 51, compressing return springs 53a, 53b to move said valve 51 to a position in which its aperture 57 is opposite orifice 11a of dosing chamber 11. In this phase, the plunger spring remains compressed.

Ejection position (Figure 15)

By continuing to press on the actuator, L-shaped element 41 releases clamp 21, and allows the liquid to be ejected via the action of return spring 14.

As indicated in the first embodiment, if the action on the actuator is interrupted, the quantity of liquid present in the chamber is re-injected into the receptacle.

Return to the rest position (Figures 16, 17 and 18)

By releasing the pressure on the actuator, in a first phase (FIG.16) the second inclined plane 35b of L-shaped element 41 is positioned behind the corresponding inclined plane 25b of clamp 21. In a second phase (FIG. 17), L-shaped element 41 tips compressing spring 47, and in a second phase (FIG. 18), L-shaped element 41 is returned to its initial position by spring 47. This return to the rest position is actuated by springs 49 compressed via the action of the actuator.

Figures 19, 19A and 20 show a variant of a second embodiment wherein a modified element is also applicable to the first embodiment.

In Figure 19, which shows the apparatus in the rest position, it can be seen that actuator 30 is extended in the direction in which pressure F is exerted by a panel 39 insulating through passage 7 from the external environment when the apparatus is not being used. Panel 39 is provided with an aperture 37 which is placed opposite through passage 7 when the ejection position is reached, as shown in Figure 20. This variant allows conditions of sterility to be increased, even if in the first embodiment the flank of the drum already forms, in the rest position, a first means for insulating the whole of the apparatus from the external environment.

Figure 19 also shows variants relative to the second embodiment whose object is to make the apparatus according to the invention more economical.

The two actuator return springs 49a, 49b are replaced by a single spring 49 disposed between the inner face of actuator 30 and unit 9 of frame 3.

It can also be seen that the body of actuator 30, its external cover 30a and panel 39 are made in a single piece. The same is true of plunger 10 as regards clamp 21 and rod 13.

Again with reference to Figure 19A, it can also be seen that L-shaped tipping element 41 has been modified and simplified, while fulfilling the same function, with, however, slightly different kinematics. Small branch 43 has been thinned so as to have sufficient flexibility to allow the L-shaped element to more aside upon return to the rest position; spring 47 has thus been omitted. It can also be seen that L-shaped tipping element 41 no longer includes pivots 45a, 45b. Said tipping element 41 is driven in translation by actuator 30 by having the end of its small arm 43 gripped in an extension 48 of the actuator, whereas the large arm 45, which still has a corner shaped end 35 with the two inclined planes 35a, 35b, slides over a vertical wall 15 of unit 9 when a pressure F is exerted on actuator 30.

It is clear that the devices described are arranged for multi-dose applicaitons, i.e. applications in which doses are repeatedly drawn from a supply and repeatedly ejected. It is also clear that the devices are exemplified with features suitable for eye treatment applications. Typical parameters for this application will be given below although the invention shall not be regarded as limited to this application or any such exemplified parameter. A typical single dose volume for delivery to the eye can be less than 100 microliter, preferably less than 50 microliter, preferably less than 25 microliter, preferably less than 15 and most preferably less than 10 microliter. Generally the volume is at least 1, preferably at least 2 and most preferably at least 3 microliter. The liquid receptacle or supply line preferably has the capacity to deliver a plurality of such doses. A suitable speed for the stream of drops or jet ejected should be a balance between on one hand enough linear momentum to traverse an air gap between opening and target, without gravity assistance, and to travel fast enough not be obstructed by blinking and on the other hand not so fast as to cause inconvenient sensible impact on the eye. The ideal speed is to some extent dependent on the drop size used but as a general rule the drops should be able to traverse at least 1 cm, preferably at least 3 and most preferably at least 5 cm through air by own momentum, incorporating reasonable distances between opening and target. A suitable lower speed limit when leaving the opening is 1, m/s, preferably at least 5 m/s and most preferably at least 10 m/s. Generally the speed is lower than 200 m/s and preferably lower than 100 m/s. A suitable drop size so defined should be sufficient not to be retarded too quickly and not to be easily redirected, e.g. to be inhaled, and preferably has a minimum diameter of 20 micron, preferably not less than 50 micron and most preferably at least 100 microns. Normally the size is less than 2000 micron and preferably less than 1500 micron. The stream may take the form of a shower or spray of atomized liquid droplets but preferably the stream is narrow and fairly coherent although even such a stream tend to break up into individual droplets after a certain time of distance. The above given values are intended to relate to spherical droplets and for multiple droplets to the weight average of particle diameters. A coherent stream tends to break up into droplets of a diameter of roughly double the diameter of the stream. Accordingly suitable opening diameters for the containers are about half the above given drop diameters or roughly between 10 and 1000 microns, preferably between 20 and 800 microns. The above considerations are fairly independent of liquid viscosity and tend to apply both for solutions and ointments. It is desirable that the whole dose can be delivered in a time shorter than the blink reflex time, i.e. in a time shorter than about 150 ms, preferably shorter than 100 ms and most preferably shorter than 75 ms.